

## **ATTACHMENT A**

### **Remarks**

The claims of the present invention were restricted between method claims, Group I, 89-122, 124-126, 128-131 and 145-153 and compound claims, Group II, claims 132-144. During the Examiner interview, the Examiner said that the restriction requirement would be withdrawn and that the compound claims would not be restricted. However, in order to expedite the present case to allowance, Applicants have canceled compound claims 132-146. Further, in order to limit the diseases and conditions treated, claims 129-131 and 153 also have been canceled. Applicants reserve the right to file a continuation application to pursue protection for the now canceled subject matter.

It is respectfully noted that the instant claims now specifically refer to the treatment of Alzheimer Disease (AD), and Memorization, Wakefulness and Attention disorders.

In addition, during the Examiner interview, the Examiner raised the issue that the Applicants must show a nexus between the claimed receptor activity and the diseases/conditions recited either through submitting articles or declarations. Further, the Examiner suggested that the method claims should have the language that an effective amount is effective to inhibit the H<sub>3</sub> receptor activity.

By this Amendment, Applicants have submitted a third Declaration of named inventor Professor Schwartz along with cited articles which evidence a nexus between the inhibition of the H<sub>3</sub> receptor and the recited diseases/conditions. Specifically, the effect of H<sub>3</sub> receptor blocking enhances the release of histamine, increases the level of tele-methylhistamine (a major histamine metabolite) and treats diseases and disorders

which benefit from activation of histaminergic neurons activity (Decl., ¶4). Further, histaminergic neurons have a well established role in AD, memorization, attention and wakefulness indicating that enhancement of histaminergic neuron activity can compensate cognitive impairment in both AD and attention, wakefulness and memorization disorders (Decl., ¶7.1 and 7.2). Based on this and the entire declaration, a nexus is established between the inhibition of the H<sub>3</sub> receptor and the recited diseases and conditions.

Further evidence of the nexus between the inhibition of the H<sub>3</sub> receptor and the recited diseases is provided in the previously submitted Declarations of January 8, 2003 and December 19, 2003, along with the cited references, copies of which are attached to this Amendment (see Decl., ¶5). Copies of the references cited in the present declaration are being filed herewith.

Additionally, experimental data disclosed in the present declaration clearly and unambiguously establish the claimed activity of the compounds of the invention in human patients (see Decl., par.10.1 to 10.3).

Human patients administered with compounds of the invention showed cognitive improvements. These results thus evidence that the compounds of the invention, acting as ligands of the H<sub>3</sub> receptor are useful for the treatment of AD and attention, wakefulness and memorization disorders.

Finally, it is also noted that the above results establish once again that the experimental results on animal obtained for a substantial number of compounds given in the specification and previous declaration are predictable of the human activity.

In view of the foregoing, Applicants respectfully submit that the present application is in condition for immediate allowance.